REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 3, 4, 6 and 8 were pending in this application when last examined.

Claims 3, 4, 6 and 8 were examined on the merits and stand rejected.

Claim 3 is amended to recite that "the composition is administered in a single daily dose". Support for this amendment can be found on page 6, lines 30-32, of the specification as filed and in claim 4 as filed. Claim 3 is also amended to remove the limitation "ingestion of the pharmaceutical composition before a meal or after a meal does not significantly alter either the bioavailability or maximum plasma concentration of the active principle" as such limitation is an inherent property of the claimed composition and therefore explicit recitation of such in the claim is unnecessary.

Claim 4 is cancelled without prejudice or disclaimer thereto.

No new matter has been added.

II. DECLARATION UNDER 37 CFR 1.132

On page 3 of the Action, the Office indicated that the Declaration submitted under 37 CFR 1.132 on February 23, 2007, was deficient because it did not compare the invention to the closest prior art. In particular, the Office contended that the closest prior art would be the art-known immediate release formulation. Applicants respectfully note that the Declaration compared 60 ml immediate release efletirizine capsules to the claimed pharmaceutical composition. Applicants note that this composition is an art-known immediate release formulation. Therefore, applicants respectfully request the Examiner to reconsider the Declaration under 37 CFR 1.132 submitted on February 23, 2007 since such Declaration does compare the closest prior art to the claimed pharmaceutical formulation.

III. OBVIOUSNESS REJECTIONS

On pages 2-3 of the Action, claims 3, 4 and 7 remained rejected under 35 U.S.C. § 103(a) as obvious over Sunshine et al. in view of Kreutner et al. New claim 8 was also included in this rejection.

On page 5, claim 6 remained rejected under 35 USC § 103 as obvious over Sunshine et al. in view of Kreutner et al. and further in view of Guy et al.

These rejections are respectfully traversed as applied to the remaining amended claims for the reasons of record and for the following reasons.

The claimed pharmaceutical compositions can be administered orally and control the release of the pharmaceutically active substance such that a single daily dose exhibits rapid therapeutic activity.

On the other hand, if the prolonged-release pharmaceutical formulations of the art are applied to efletirizine, such formulations exhibit delayed effective plasma concentrations and therefore delay the therapeutic action of the active principle.

The claimed invention concerns a combination of a fraction which allows immediate release of the active principle with a second fraction which allows prolonged release of the active principle. This combination makes it possible to satisfy the specific pharmacokinetic requirements related to the use of efletirizine and to minimize variations in bioavailability and maximum plasma concentrations associated with having a meal just prior to ingestion of the pharmaceutical. Moreover, after intense research, the present inventors have found the necessary balance between immediate release of the active principle and prolonged release of the active principle for maintaining an effective dose of the active principle for a full day while avoiding reaching plasma concentration peaks associated with side effects.

The present inventors have also shown that by combining at least one immediate-release fraction and at least one prolonged-release fraction, the pharmaceutical compositions thus obtained are resistant to variations in bioavailability and maximum plasma concentrations caused by ingestion of a meal prior to ingestion of the

pharmaceutical composition. This unexpected and inherent property of the claimed invention is shown in Example 5 on page 22 of the specification. This property is not observed for immediate-release compositions as demonstrated in Example 4 on page 20 of the specification. Furthermore, this property of the claimed pharmaceutical composition is surprising and unexpected as indicated by the 37 C.F.R. § 1.132 Declaration submitted February 23, 2007. As a result of this inherent property, the consequences of incorrect handling or use by a patient of the claimed composition are reduced.

Furthermore, the claimed invention, as amended, relates to a modified-release pharmaceutical composition for administering an effective amount of efletirizine as a single daily dose.

A skilled artisan could not look to the literature and effectively compare efletirizine with other antihistamines such as loratadine and cetirizine, due to efletirizine's very specific pharmacokinetic characteristics (including half-life, plasmatic elimination, oral clearance, etc.) For example, loratadine is a long acting drug exhibiting a dose-related rapid onset inhibition of the histamine-induced skin wheal and flare response in humans. Loratadine is apparent in the plasma 2 hours after ingestion and persists throughout the 24 hour observation period. The loratadine elimination half-life (t 1/2b) ranges from 7.8 to 11 hours; the descarboethoxyloratadine half-life ranges from 17 to 24 hours; and the cetirizine half-life ranges from 6.5 to 10 hours. Thus, these antihistamines already possess pharmacokinetic characteristics suitable for single daily doses and a skilled artisan would not examine such literature for obtaining daily dose pharmaceuticals containing principals with significantly shorter half-lives such as efletirizine, which has a half-life of 2.5 to 3.5 hours.

Efletirizine, unlike loratadine, does not persist throughout the 24-hour observation period. Consequently, a very specific galenic composition is required to obtain a daily dose tablet. Moreover, due to the pharmacokinetic characteristics of loratadine, a skilled artisan cannot merely replace loratidine with efletirizine in a galenic composition containing loratadine as an active ingredient and obtain a similar pharmacokinetic profile.

Applicants therefore respectfully suggest that neither Sunshine et al. in view of Kreutner et al nor Sunshine et al. in view of Kreutner et al. and further in view of Guy et al. teach or suggest the claimed daily dose efletirizine composition with the unexpected inherent property of resistance to variation in bioavailability and maximum plasma concentration of the active principle caused by ingestion of a meal prior to ingestion of the claimed pharmaceutical composition. Furthermore, none of the cited references teach or suggest that a principal with a short half life, such as efletirizine, can be used as a daily dose tablet that maintains an effective dose of the active principle for a full day while avoiding reaching plasma concentration peaks associated with side effects. Applicants therefore respectfully suggest that these rejections, as applied to the remaining amended claims, are untenable and should be withdrawn.

IV. INDEFINITENESS REJECTION

On page 6 of the Action, claims 3, 4, 6 and 8 were newly rejected under 35 USC § 112, second paragraph, as indefinite for the phrase "does not significantly alter either the bioavailability or maximum plasma concentration".

Applicants respectfully submit this rejection is overcome as applied to the remaining amended claims for reasons which are self-evident.

CONCLUSION

In view of the forgoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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